Armed Forces College of Medicine

AFCM

Glomerular Filtration

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Enumerate the general functions of the kidney.
2. Define the basic renal processes that result in urine formation .
3. Describe how glomerular filtrate is formed and composition of this filtrate .
4. Describe the structural components of the filtration barrier and the main determinants soluble.
5. Define glomerular filtration rate and state its normal value .
6. List the forces involved in glomerular filtration and their normal values .
7. List the factors that affect GFR .
8. Describe the factors that affect glomerular filtration rate .
9. Analyse the results of GFR.

Overview of Renal Function

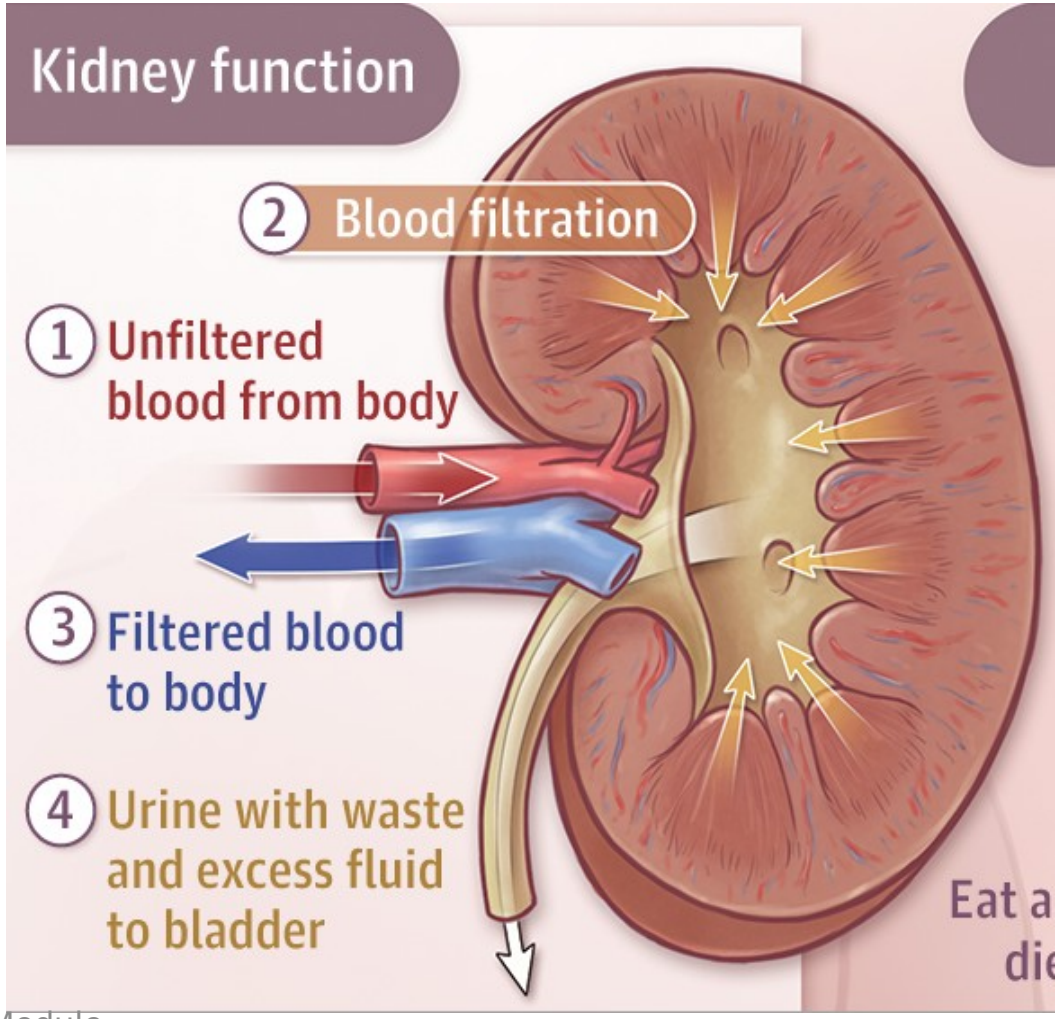
- **The kidneys are both excretory and regulatory organs .**
- **Because of the kidney's homeostatic functions, the tissues and cells of the body are able to carry out their normal functions in a relatively constant environment.**

What are the functions of the kidney?

1. Regulation of water and electrolyte balance.

2. Excretion of metabolic waste products as urea, uric acid, creatinine.

3. Excretion of foreign chemicals, e.g. drugs, food additives and pesticides.



https://jamanetwork.com/journals/jama/fullarticle/2524

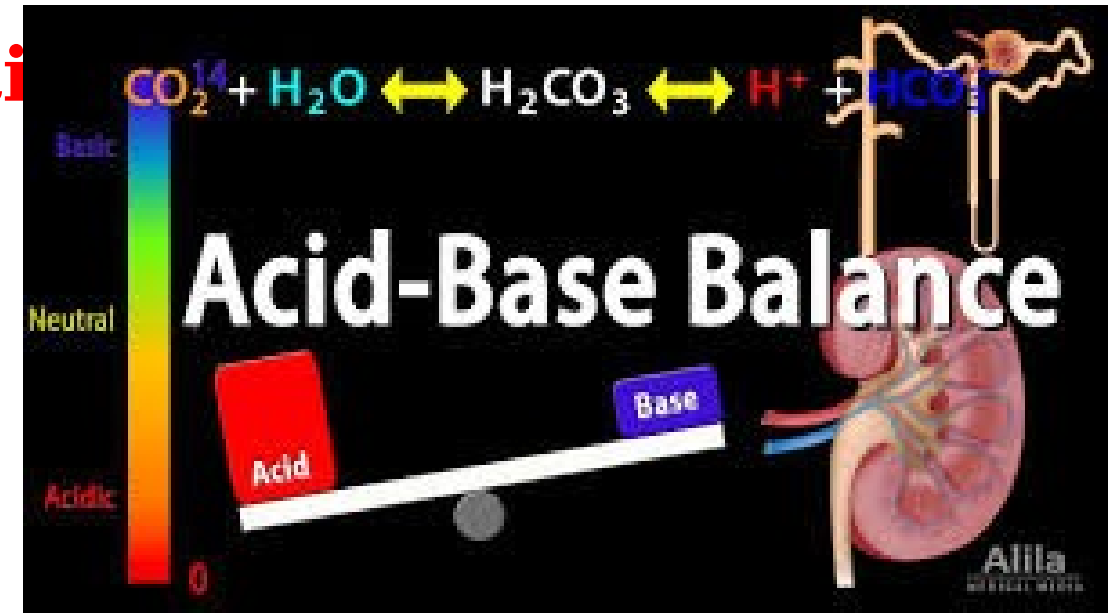
4. Regulation of arterial blood pressure:

I. Short-term regulation: renin-angiotensin aldosterone system.

II. Long-term regulation: through excreting variable amounts of sodium and water.

5. Regulation of acid-base balance by:

a) Elimination of acids produced from the metabolism of proteins such as sulphuric and phosphoric acid.

b) Regulati 

the body.

6. Gluconeogenesis:

The kidneys synthesize glucose from amino acids during prolonged fasting and add it to the blood. This helps to maintain blood glucose concentration.

7. Secretion of prostaglandins (PGE2, PGl2) and bradykinins.

These act as paracrine hormones that play important role in regulation of the renal blood flow.

8- Endocrine functions of the kidney:

a. Regulation of erythrocyte production .

b. Regulation of 1,25-Dihydroxy vit. D_3 production.

c. Renin secretion.

Basic Function of The Nephron

nephron is capable of forming urine by three processes:

1) Glomerular filtration:

Filtration from the glomerular capillaries into Bowman's capsule of a fluid that is nearly free of proteins. Ultrafiltrate

2) Tubular reabsorption:

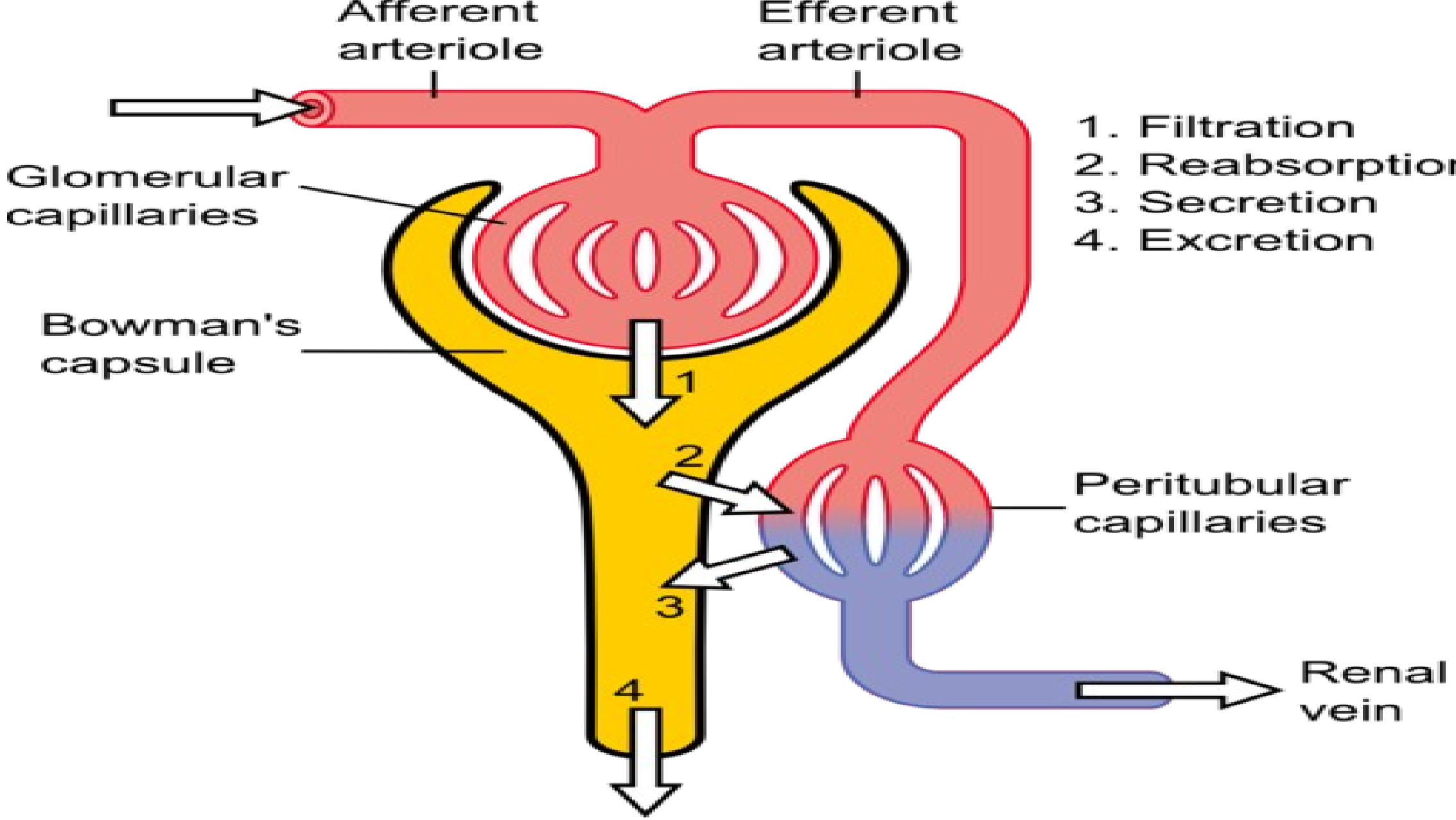
It is the transfere of water and solutes from the filtrate back into the blood of the peritubular capillaries.

3) Tubular secretion:

It is the transfer of solutes from the peritubular capillaries into the tubular lumen

- The rate at which different substances are excreted in urine represents the sum of the three processes.

Urinary excretion rate = **Filtration rate** − **reabsorption rate** + **secretion rate**



Excretion = Filtration − Reabsorption + Secretion

Glomerular Filtration

20 % Of the plasma flowing through the kidneys is filtered by the glomerular capillaries into Bowman’s capsule. The filtered fluid is called Glomerular filtrate.

Composition of the Glomerular filtrate:-

Glomerular filtrate is protein-free ultrafiltrate of plasma i.e. plasma- colloids.

Glomerular membrane

The membrane that separates the blood in the glomerular capillaries from the Glomerular filtrate in Bowman’s capsule is formed of three layers

The capillary endothelium'

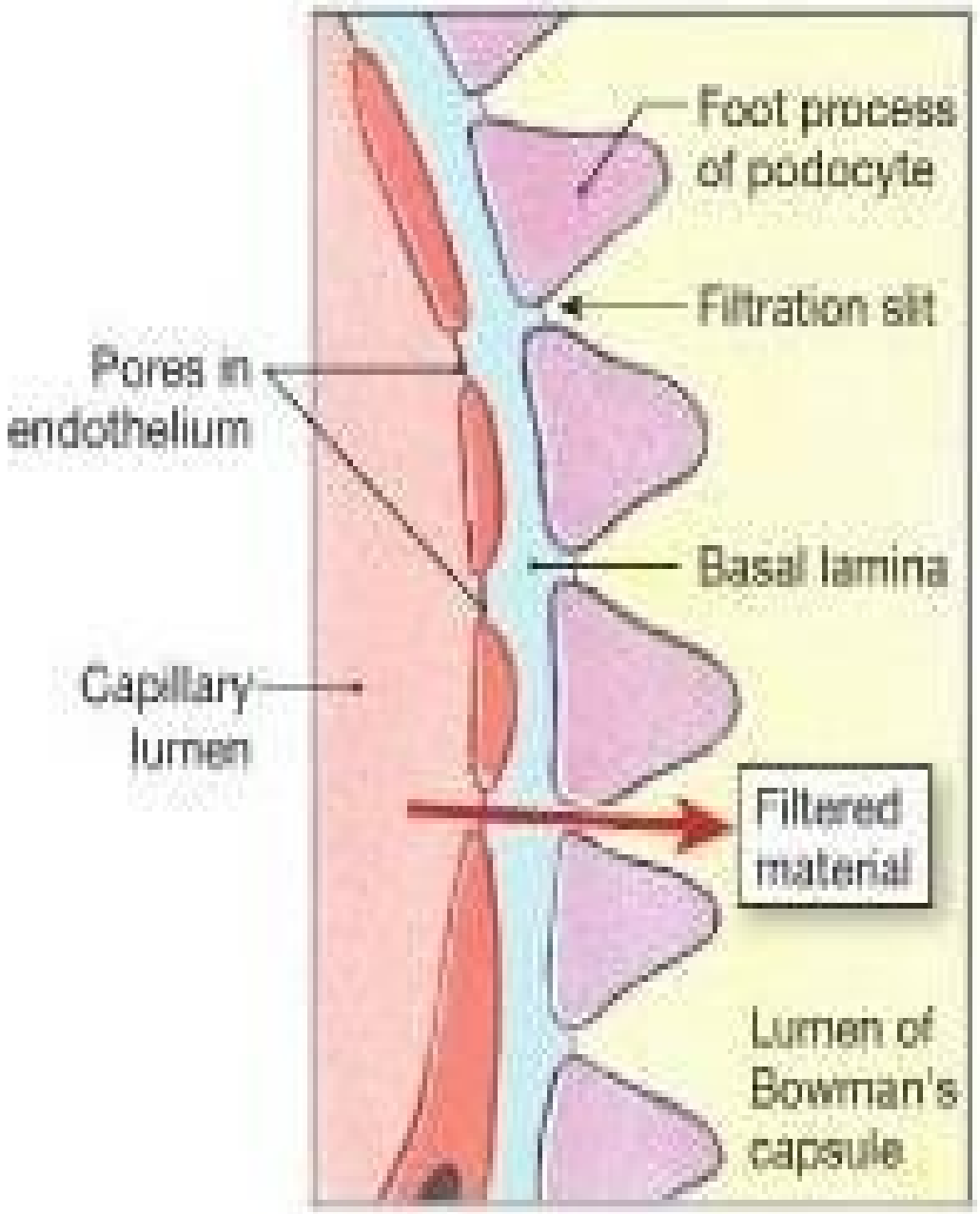
It is perforated by small holes called fenestrae. This layer does not act as a major barrier for plasma proteins as the fenestrations are relatively large (70-90 nm in diameter).

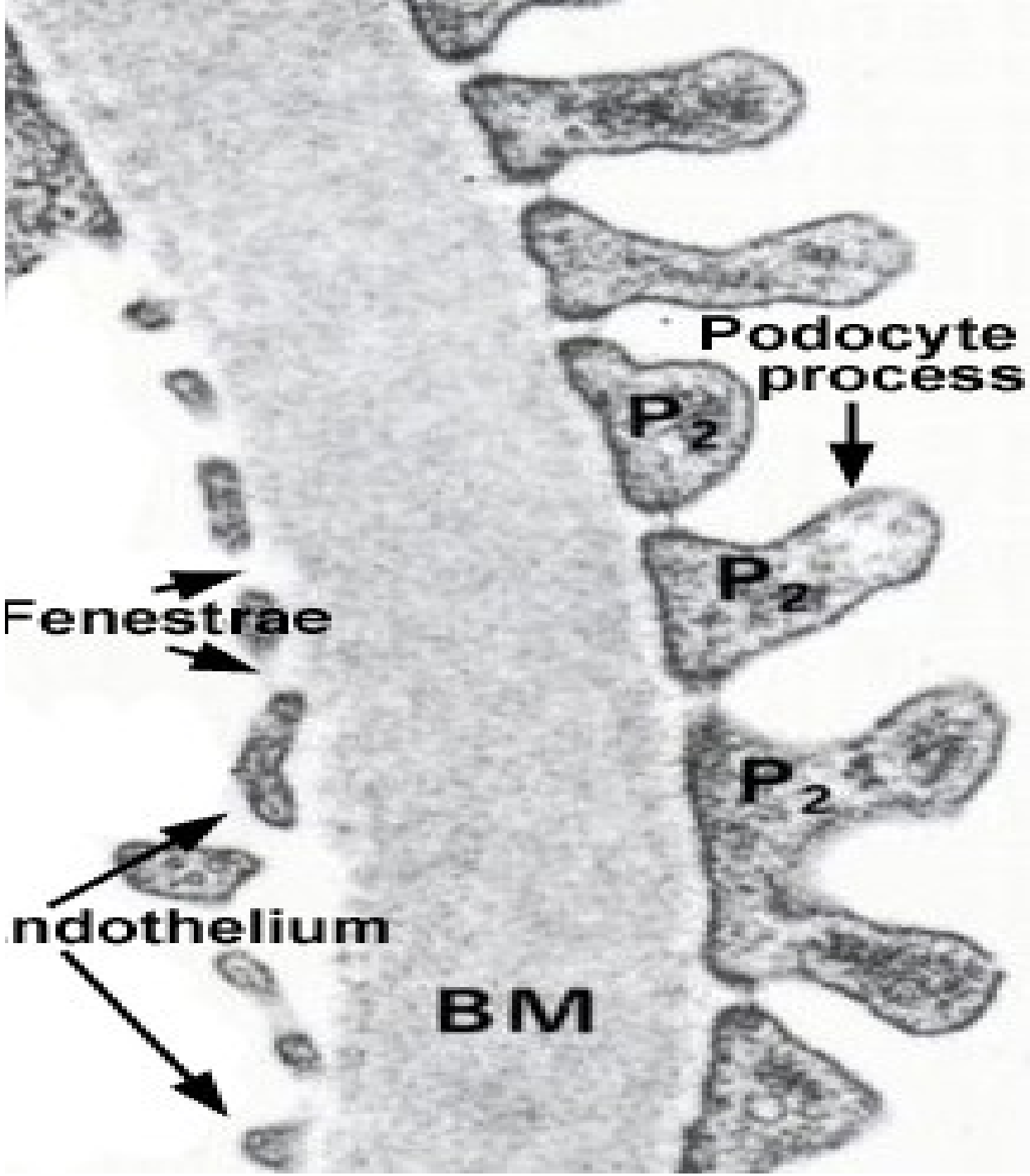
Basement membrane:

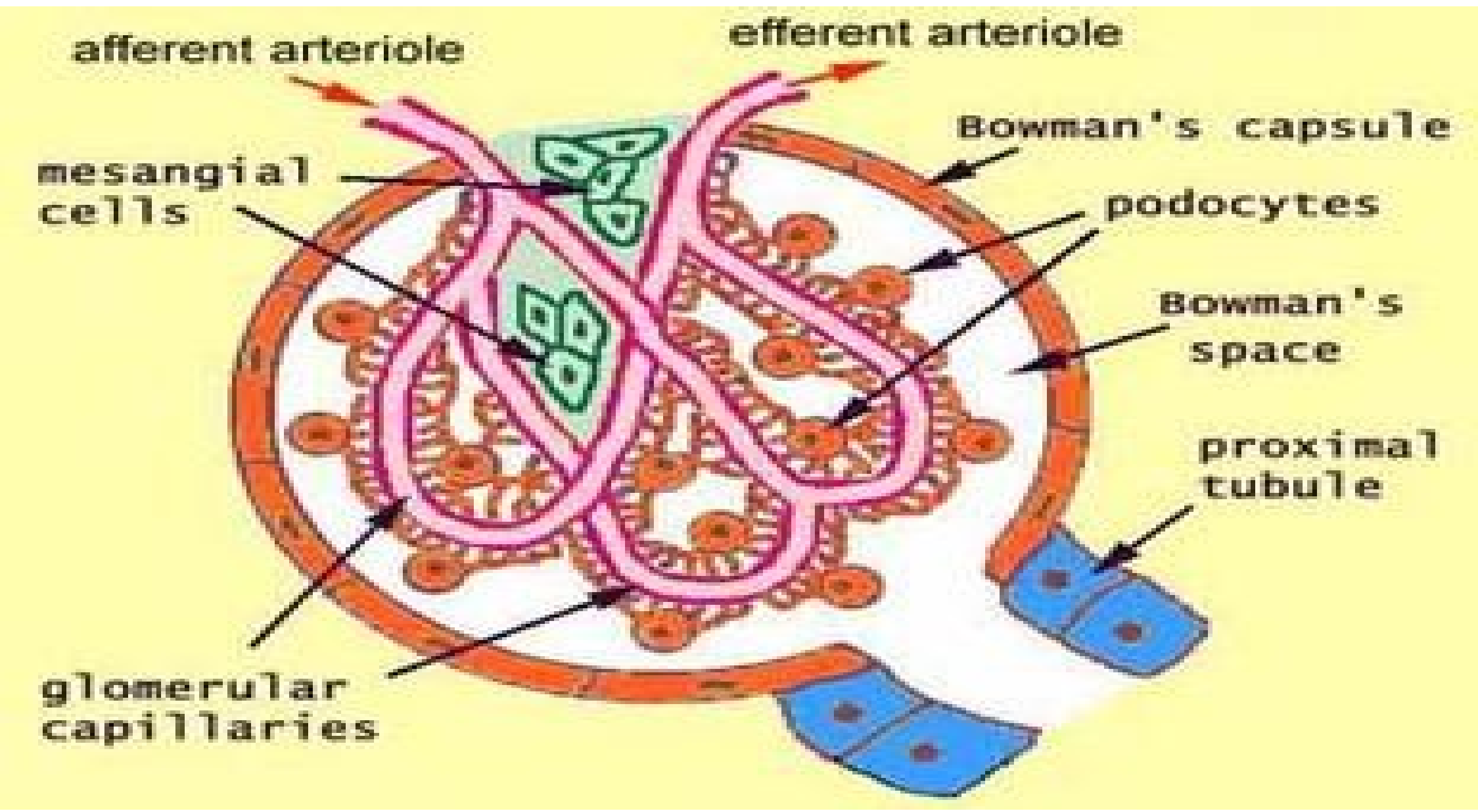
It consists of a meshwork of collagen and proteoglycan fibrillae that have large spaces. The proteoglycan carry strong negative electrical charges, therefore, the basement membrane prevents effectively filtration of plasma proteins, .

Podocytes:

These are epithelial cells that lie on the outer surface of the glomerulus. They have numerous pseudopodia that interdigitate to form slit pores (25 nm wide


Foot process of podocyte
Filtration slit
Pores in endothelium
Basal lamina
Capillary lumen
Filtered material
Lumen of Bowman's capsule


Podocyte process
P2
P2
P2
Fenestrae
ndothelium
BM

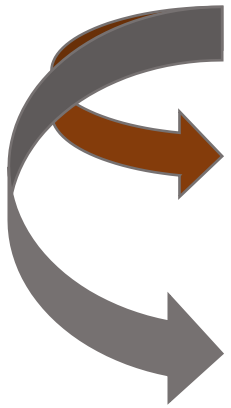

afferent arteriole
efferent arteriole
Bowman's capsule
mesangial cells
podocytes
Bowman's space
proximal tubule
glomerular capillaries

Permeability of the glomerular membrane

- The permeability of the glomerular capillaries is about 50 times that of the capillaries in skeletal muscle.

- it is highly selective in determining which molecules will filter.

- This high selectivity is determined by:



1) Size of the solutes.

2) Electric change of the solute.

Size of the Solute

❖ Neutral substances with molecular diameter of less than 4 nm are freely filtered and the filtration of neutral substances with diameter of more than 8 nm is zero.

❖Between these values, filtration is inversely proportionate to diameter .

❖The permeability of the glomerular membrane to solutes decreases with increasing the molecular diameter.

Charge of the Solute

❖Negatively charged molecules are filtered less easily than positively charged molecules of equal molecular diameter due to the negative charges in the basement membrane .

❖This may explain why albumin with effective molecular diameter of approximately 7 nm, has a glomerular concentration only 0.2% of its plasma concentration than the higher concentration that would be expected on the basis of diameter alone (Circulating albumin is negatively charged).

❖In certain kidney diseases, the negative charges on the basement membrane is lost leading to albuminuria.

Glomerular Filtration Rate (GFR)

Definition:

Volume of the glomerular filtrate formed by the glomeruli of both kidneys per minute.

Normal GFR:

- The GFR in an average - sized normal man is approximately 125 ml/min.
- Values in women are 10% less than those in men.
- Both plasma creatinine and urea increase when GFR decreases.
- GFR decreases with age, although plasma creatinine remains constant.

Control of GFR

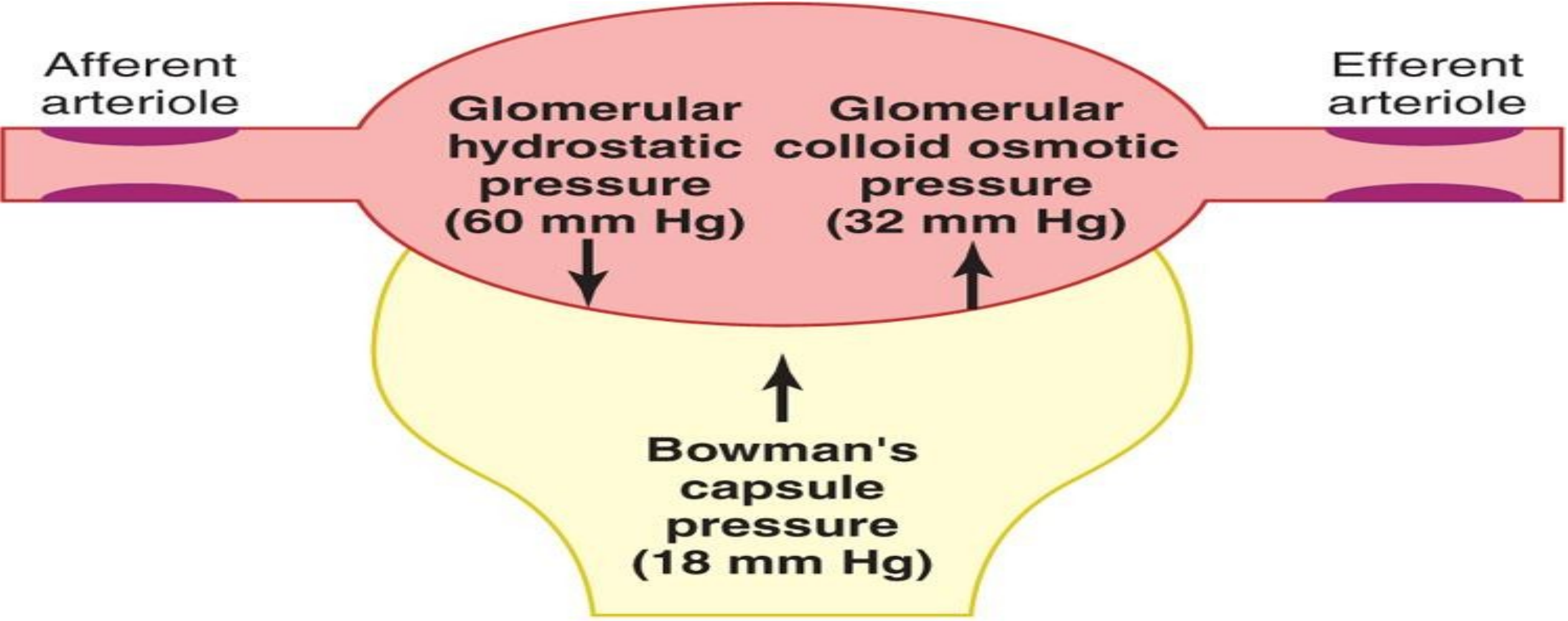
- The factors govering filtration across the glomerular capillaries are the same as those govering filtration across all other capillaries.

- *<u>These factors are summarized by the Starling equation:</u>*

$$\text{The GFR} = K_F\,(HP_GC - HP_{BC}) - (\pi GC - \pi_{BC})$$
$$= K_F\,(HP_{GC} - HP_{BC} - \pi_{GC} + \pi_{BC})$$

Where

- HP_{GC} → The mean hydrostatic pressure in the glomerular capillaries (mmHg).
- HP_{BC} → The mean hydrostatic pressure in Bowman's capsule (mmHg).
- π_{GC} → The osmotic pressure of plasma proteins in the glomerular capillaries (mmHg).
- π_{BC} → The osmotic pressure of proteins in the filtrate (mmHg).



Net filtration pressure (10 mm Hg) = Glomerular hydrostatic pressure (60 mm Hg) − Bowman's capsule pressure (18 mm Hg) − Glomerular oncotic pressure (32 mm Hg)

Forces favouring filtration (mmHg)

1) HP_{GC}= 60 mmHg.
2) π_{BC} = 0 mmHg.

Forces opposing filtration (mmHg):

1) HP_{BC}= 18 mmHg.
2) π_{GC} = 32 mmHg.

The net filtering pressure = 60 - 18 – 32 = 10 mmHg.

Factors that affect GFR

- From Starling equation, variations in the factors involved have predectable effect on GFR.

$$GFR = K_F \times (HP_{GC} - HP_{BC}) - (\pi_{GC} - \pi_{BC})$$

1- Changes in ultrafiltration coefficient (K_f):

K_f: An increased Kf raises the GFR where a decrease in Kf reduces the GFR.

Factors that affect GFR

K_F depends on:

1. Permeability of the glomerular membrane
2. Surface area of the glomerular membrane

Glomerular ultrafiltration co-efficient = 12.5 ml/min/ mrnHg

Factors that affect GFR

1) Surface area of the glomerular capillaries:

a) Contraction of mesangial cells will reduce the surface area available for filtration; as contraction at points where the capillary loops bifurcate shifts the blood flow from some glomerularcapill aries

The following agents cause contraction of the mesangial cells and therefore ***decrease GFR***

- Vasopressin
- Norepinephrine
- ThromboxaneA2
- Histamine
- Leucotrines A and D
- Endothelins
- PGF2

Factors that affect GFR

- cAMP
- PGE2
- ANP
- Dopamine

c) Some diseases lower K_F by reducing the number of the functional glomerular capillaries, with reduction of surface area for filtration e.g. chronic uncontrolled diabetes mellitus2) Permeability: Increasing the thickness of the glomerular capillary membrane will reduce its permeability e.g. in chronic uncontrolled diabetes mellitus and hypertension.

Factors that affect GFR

2- Changes in the glomerular capillary hydrostatic pressure:

Increases in glomerular hydrostatic pressure raise GFR, whereas decrease in HP_{GC} reduce GFR:

Glomerular hydrostatic pressure is determined by:

1. Diameter of the afferent arteriole:

a) Vasodilatation of the afferent arteriole ++ HP_{GC} ++ GFR

e.g. bradykinins, PGE_2 and PGI_2 .

b) Vaso-constriction of the afferent arteriole e.g. by noradrenaline during sympathetic stimulation decrease HP_{GC} decrease GFR..

The increased sympathetic activity that occurs during exercise may reduce GFR to less than 50% of normal.

Factors that affect GFR

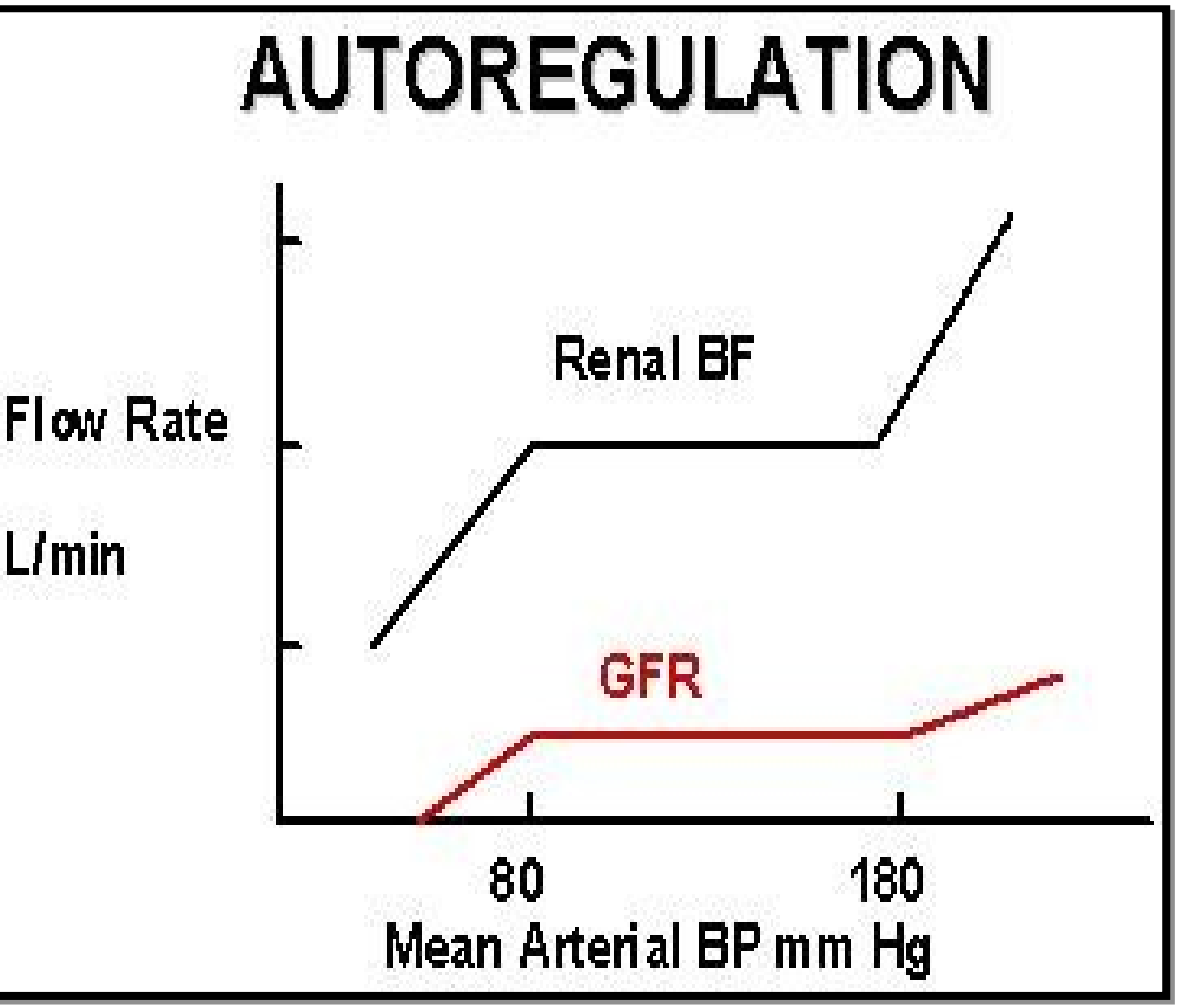
2. Diameter of the efferent arteriole:

a) Moderate vasoconstriction of the efferent arteriole increases the resistance to the outflow from the glomerular capillaries. This raises the HP_{GC} slight increase of GFR. e.g. angiotensin II.

b) Severe constriction of the efferent arteriole will reduce renal blood flow reduce GFR.

Factors that affect GFR

3. Arterial blood pressure:



- The renal blood flow and GFR are kept relatively constant despite marked changes in arterial blood pressure (between 90-220 mmHg) by autoregulatory mechanisms.

- Increased arterial pressure tends to raise HP_{GC} and to increase GFR. However, this effect is buffered by autoregulatory mechanisms. However, when the mean systemic pressure drops below 75 mmHg, there is a sharp drop in GFR

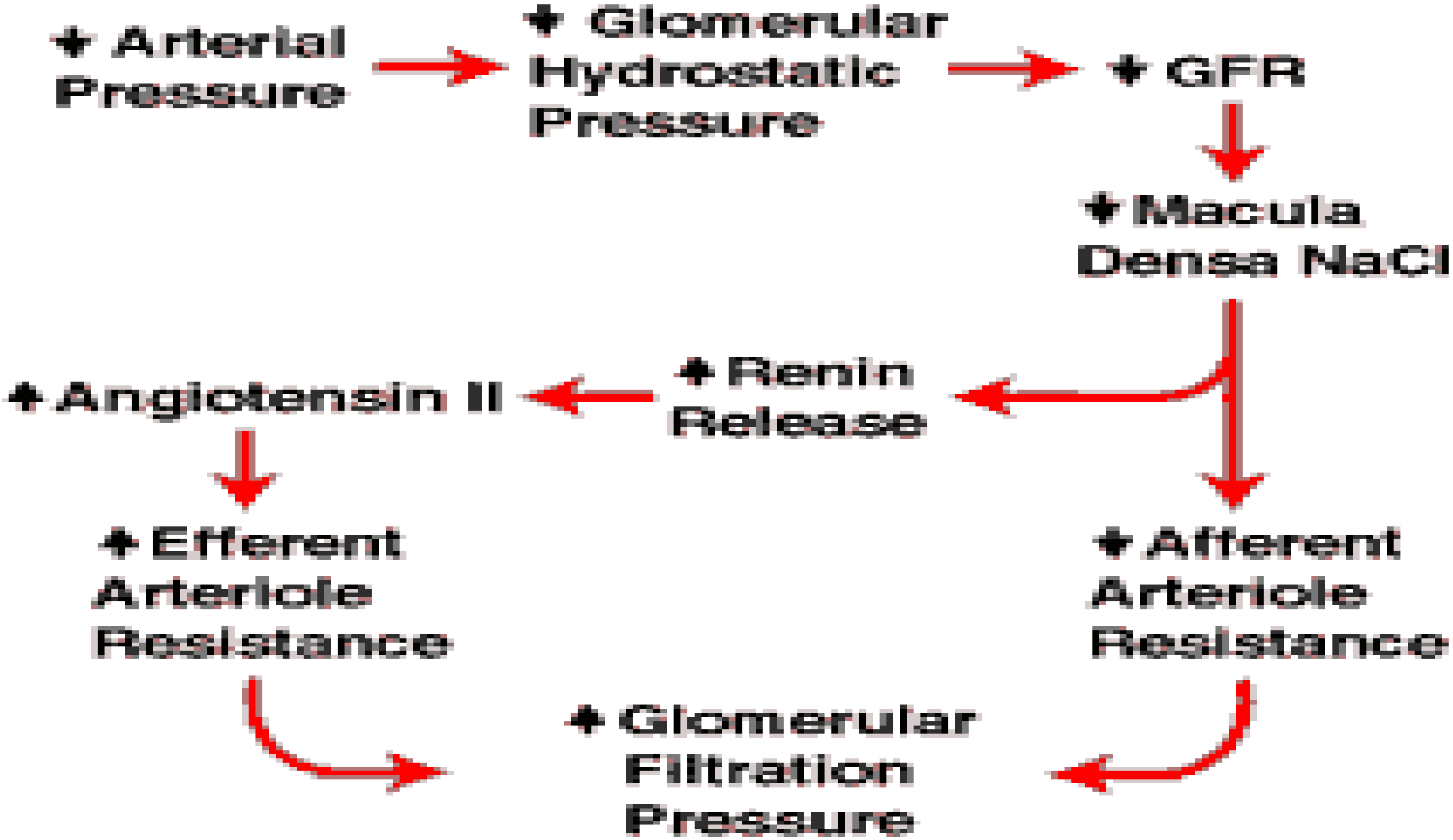
Mechanisms of Autoregulation

•a) Tubulo-glomerular feed back:

i)When renal arterial pressure increases both RBF and GFR increase.

•The increase in GFR results in increase delivery of solutes and water to the macula densa.

•The macula densa responds to increased delivered solute load by secreting the vaso- active substance; adenosine that produces vasoconstriction of afferent arterioles, reduces RBF, HP_{GC} and GFR back to normal.


↑ Arterial Pressure
↑ Glomerular Hydrostatic Pressure
↑ GFR
↑ Macula Densa NaCl
↑ Afferent Arteriole Resistance
↑ Renin Release
↑ Angiotensin II
↑ Efferent Arteriole Resistance
↑ Glomerular Filtration Pressure

Mechanisms of Autoregulation

ii) Conversely with drop of arterial blood pressure the HP_{GC} tends to drop.

- The GFR decreases.

- Flow rate in the loop of Henle decreases, so that reabsorption of sodium and chloride ions in the ascending loop of Henle increases.

- Sodium chloride reaching the macula densa decreases. Macula densa sends signals to:

-Afferent arteriole: producing dilatation which raises HP_{GC} and help to return GFR towards normal.

- Efferent arteriole: producing constriction. This occurs though

Mechanisms of Autoregulation

b) Myogenic Autoregulation:

- Discussed before in regulation of renal blood flow.

- This response is rapid and it is the first line of defense against rapid change in blood pressure. An increase in ABP results in stretching of the afferent arteriolar wall contraction of the smooth muscles and returns the diameter towards normal to minimize change in glomerular capillary pressure.

- Conversely a decrease in ABP results in relaxation of smooth muscle.

Factors that affect GFR

III. Changes in Bowman's Capsule Hydrostatic Pressure:

-Increasing HP_{BC} reduces GFR.

- A stone in the ureter that obstructs the outflow of urine from the ureter will decrease GFR by raising HP_{BC}.

Factors that affect GFR

IV. Changes in the glomerular colloid osmotic pressure:

-Changes in the concentration of plasma proteins affect GFR as follows:

1. An increase in π_{GC} e.g. in dehydration will decrease GFR.

2. A decrease in π_{gc} *e.g. in cases of hypoproteinemia will increase GFR.*

Factors that affect GFR

V. Renal Vasodilators:

- PGE_2, PGI_2 and bradykinin produce renal vaso-dilatation, and increase in renal blood flow and GFR.

- Administration of anti-inflammatory drug like aspirin that block PG synthesis may cause marked reduction in GFR.

- Prostaglandin synthesis in the kidneys in increased by sympathetic nervous system stimulation and angiotensin II. This may protect the renal vessels from severe vasoconstriction during high sympathetic activity and elevated angiotensin II in situation of severe cardiovascular

Factors that affect GFR

VI. Effect of protein intake:

- High protein intake increases renal blood flow and GFR.

Mechanism:

High protein intake rise of amino acids into the blood filter in Bowman's capsule.

- Increased amino acids reabsorption stimulates sodium reabsorption in the proximal tub .

Lecture Quiz

Question 1

Use the values below to answer the following question .

Glomerular capillary hydrostatic pressure = 47 mmHg

Bowman's space hydrostatic pressure = 10 mmHg

Bowman's space oncotic pressure = 0 mmHg

At what value of glomerular capillary pressure would glomerular filtration stop ?

a) 57 mmHg
b) 47 mmHg
c) 37 mmHg
d) 10 mmHg
e) 0 mmHg

Question 2

A large increase in GFR would be expected to occur following :

a) An increase in mean arterial pressure from 90 to 140 mmHg
b) Strong sympathetic stimulation to the kidney
c) Contraction of mesangial cells
d) Substantial increase in renal blood flow .
e) Dehydration

SUGGESTED TEXTBOOKS

1. Ganong’s Review of Medical Physiology 25 th Edition from page 676 to 678
2. TEXTBOOK OF Medical Physiology 11th Edition GUYTON & HALL
3. Page 314 - 325


Thank you